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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/543,078	07/21/2005	Michinori Kohara	382.1047	7140

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EXAMINER	
PITRAK, JENNIFER S	

ART UNIT	PAPER NUMBER
1635	

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09/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/543,078	KOHARA ET AL.	
	Examiner	Art Unit	
	Jennifer Pitrak	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *9,10,14 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,11-13 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/21/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Invention I (claims1-12 and 14-16) and SEQ ID NO: 23 in the reply filed on 07/30/07 is acknowledged.

Claims 9, 10, 14, and 15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 07/30/07.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see, for example, line 11 on p. 6 of the specification). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

Claim 8 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 8 refers to the oligonucleotide of claim 7 without adding any further limitations.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 5 refers to a PNA "which is a double-stranded RNA," rendering the claim indefinite because PNAs are not RNAs.

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6-8, 11, 12, and 16 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Wakita, *et al.* (1999, J. Med. Virol., v.57:217-222).

The claims are to an oligoribonucleotide (oligo) or peptide nucleic acid (PNA) that hybridizes to the RNA of a Hepatitis C Virus (HCV) (claims 1 and 12), wherein the oligo or PNA hybridizes with the HCV RNA under stringent conditions (claim 2). The claims are also to the oligo or PNA of claim 1, wherein the sequence is a 5'-non-coding region of the RNA of HCV (claim 3), wherein the oligo or PNA hybridizes with the sequence of a highly identical region of the genetic sequences of a plurality of types of HCV different in genotype (claim 4), or wherein the oligo or PNA has a chain length of 19 to 23 base pairs (claim 6). The claims are also to a vector that expresses the oligo of claim 1 (claims 11 and 16). The claims are also to an oligonucleotide having a nucleotide sequence shown in SEQ ID NO: 23 (claims 7 and 8).

Claims 7 and 8 encompass oligonucleotides of any length that contain any 2- to 20-nucleotide sequence from SEQ ID NO: 23.

Wakita, *et al.* teach antisense HCV RNA-expressing vectors, which express RNA that hybridizes to the 5' non-coding region of HCV, and which contains a chain length of 19-23 b.p. See, in particular, "pAS TH402-335" in Figure 1b on p.218. The 5'-UTR region to which the antisense RNA hybridizes is highly identical to the genetic sequences of a plurality of types of HCVs as is disclosed in Wakita and Wands (1994, J. Biol. Chem., v.269:14205-14210), which is cited by Wakita, *et al.* (1999) in the first column on p.218. Wakita and Wands on p.14205 on the top of the right column recite that "the 5' non-coding region is highly conserved among the HCV genotypes isolated from various regions of the world." Wakita, *et al.* also disclose the HCV-expression construct, "pcDNA TH" in Figure 1a on p.218, which encodes HCV RNA containing SEQ ID NO:23. Thus, Wakita, *et al.* anticipates all of claims 1-4, 6-8, 11, 12, and 16.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seki, *et al.* (1994, CA2104649) and Bass (2001, Nature v.411:428-429).

Claims 1-4, 6-8, and 12 are described above. Claim 5 is to the oligonucleotide or PNA of claim 1 which is double-stranded RNA. SEQ ID NO: 23 of claims 7 and 8 is disclosed in the

specification on pp. 12-13 as the sense strand of an siRNA duplex. Claims 7 and 8 encompass oligonucleotides of any length that contain any 2- to 20-nucleotide sequence from SEQ ID NO: 23.

Seki, *et al.*, teach an antisense nucleotide targeting HCV and complementary to SEQ ID NO:23 and that is 20 nucleotides in length. Seki, *et al.* disclose antisense oligonucleotides useful as antiviral agents (see abstract) and particularly disclose SEQ ID NO:83, which is complementary to nucleotides 2-20 of the instant SEQ ID NO:23. The instant SEQ ID NO:23 consists of nucleotides 325-344 of the HCV genome (accession no. AY045702), which corresponds to the 5'-UTR. Seki, *et al.* do not disclose double-stranded RNA oligonucleotides.

Bass teaches on page 429, first column, that RNA interference is a routinely used gene silencing technique that has proven to be more robust than antisense techniques by working more often, decreasing expression to lower levels than antisense oligonucleotides, and working at concentrations several orders of magnitude below the concentrations typically used in antisense experiments.

It would have been obvious to one of ordinary skill in the art at the time the invention to make an siRNA (double-stranded RNA) targeting the region of HCV corresponding to SEQ ID NO:23 for the purpose of reducing HCV expression. Bass provides a motivation to make a double-stranded RNA instead of an antisense oligonucleotide by teaching that RNA interference is more robust than antisense techniques by decreasing expression to lower levels and working at much lower concentrations than antisense. Based on the motivation provided by Bass to use double-stranded RNA instead of antisense compounds to down-regulate target gene expression, one of ordinary skill in the art would recognize that targeting HCV with an siRNA corresponding

to SEQ ID NO:23 would be a more effective antiviral agent than just the antisense taught by Seki, *et al.* One of ordinary skill in the art would have had a reasonable expectation of success in making and using an siRNA to reduce HCV expression because Bass teaches RNAi using dsRNA is a more specific and more potent method than antisense. Thus, the invention of claims 1-8 and 12 would have been obvious, as a whole, at the time of the invention.

Closing

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Pitrak whose telephone number is 571-270-3061. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

J. DOUGLAS SCHULTZ, PH.D.
SUPERVISORY PATENT EXAMINER